Oscar Clinical Guideline: Elevidys (delandistrogene moxeparvovec-rokl) (PG160, Ver. 1)

Elevidys (delandistrogene moxeparvovec-rokl)

Disclaimer

Clinical guidelines are developed and adopted to establish evidence-based clinical criteria for utilization management decisions. Clinical guidelines are applicable according to policy and plan type. The Plan may delegate utilization management decisions of certain services to third parties who may develop and adopt their own clinical criteria.

Coverage of services is subject to the terms, conditions, and limitations of a member's policy, as well as applicable state and federal law. Clinical guidelines are also subject to in-force criteria such as the Centers for Medicare & Medicaid Services (CMS) national coverage determination (NCD) or local coverage determination (LCD) for Medicare Advantage plans. Please refer to the member's policy documents (e.g., Certificate/Evidence of Coverage, Schedule of Benefits, Plan Formulary) or contact the Plan to confirm coverage.

Summary

Duchenne muscular dystrophy (DMD) is an X-linked genetic disorder characterized by progressive muscle weakness and wasting due to lack of dystrophin protein. It primarily affects males, with onset around 2-5 years old. As the disease progresses, patients experience loss of ambulation, respiratory and cardiac complications, and premature death. There is no cure for DMD. Current management focuses on glucocorticoids to slow progression, supportive care, and emerging gene targeted therapies.

Elevidys (delandistrogene moxeparvovec-rokl) is an adeno-associated virus serotype-9 vector gene therapy designed to deliver a functional version of the dystrophin gene to muscle cells. While promising, larger randomized controlled trials with longer follow up are needed to further evaluate efficacy and long-term safety of Elevidys (delandistrogene moxeparvovec-rokl) for DMD.

- Currently, the FDA has granted accelerated approval to Elevidys for the treatment of ambulatory pediatric patients aged 4 through 5 years with Duchenne muscular dystrophy (DMD) with a confirmed mutation in the DMD gene. This indication is approved under accelerated approval

based on expression of Elevidys micro-dystrophin in skeletal muscle observed in patients treated with Elevidys. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).

Definitions

"**Accelerated approval**" is a pathway by the FDA to allow earlier approval of drugs that treat serious conditions and fill an unmet medical need, based on surrogate or intermediate endpoints.

"**Adeno-associated virus (AAV)**" is a type of virus that can be used to deliver genetic material into cells during gene therapy.

"**Ambulation**" refers to the ability to walk without assistance.

"**Anti-AAV antibodies**" are proteins produced by the immune system in response to the AAV vector used in some gene therapies. These can potentially limit the effectiveness of future AAV-based gene therapies.

"**Biomarkers**" are measurable indicators of the severity or presence of a disease.

"**Blinded studies**" are clinical trials in which participants do not know whether they are receiving the experimental treatment or a placebo.

"**Duchenne muscular dystrophy (DMD)**" is a genetic disorder characterized by progressive muscle degeneration and weakness. It is caused by an absence of dystrophin, a protein that helps keep muscle cells intact.

"**Dystrophin**" is a protein necessary for muscle strength and function. Its absence or dysfunction leads to the muscle degeneration seen in DMD.

"**Gene therapy**" is a technique that aims to treat or prevent disease by replacing, adding, or editing genes within an individual's cells.

"**Glucocorticoids**" is a class of steroid hormones that can reduce inflammation and alter the immune response. They are used in DMD to slow the progression of the disease.

"**Micro-dystrophin**" is a smaller but functional form of the dystrophin protein, which gene therapies like Elevidys aim to introduce to patients' muscles.

"**North Star Ambulatory Assessment (NSAA)**" is a validated measure to assess ambulatory function in DMD patients.

"**Open-label**" is a type of clinical trial where both the researchers and the participants know which treatment is being administered.

"**Placebo-controlled trial**" is a study where the effect of a drug is compared with a placebo (a substance with no therapeutic effect).

"**Primary & Secondary endpoints**" are specific outcomes that a clinical trial is designed to measure, determining the effectiveness and side effects of a treatment.

"**Randomized controlled trials**" are clinical studies where participants are assigned to groups randomly, with one group receiving the treatment and the other a control (like a placebo).

"**X-linked**" is a mode of inheritance where the gene causing the condition is located on the X chromosome.

Policy Statement on Elevidys (delandistrogene moxeparvovec-rokl) Efficacy Information

There is insufficient evidence to indicate that Elevidys (delandistrogene moxeparvovec-rokl) provides clinically meaningful benefits that outweigh the potential risks for patients with Duchenne muscular dystrophy (DMD). The Plan considers Elevidys (delandistrogene moxeparvovec-rokl) to be not medically necessary for DMD at this time, as it is deemed to be experimental, investigational, or unproven.

Based on review of the available data from three clinical trials of Elevidys in ambulatory boys aged 4-7 years old with DMD, overall efficacy data are insufficient to conclude that Elevidys provides a clinically meaningful therapeutic effect for DMD.:

1. Trial #1: SRP-9001-101 (Study 101, NCT03375164) provided initial data on Elevidys in a small cohort of young boys with DMD.
    - Study 101 was an open-label, single-arm, first-in-human study of Elevidys in 4 ambulatory boys aged 4-6 years with Duchenne muscular dystrophy (DMD).

- The primary objective was to assess safety. Secondary objectives included evaluating Elevidys micro-dystrophin expression, Bayley-III Gross Motor Subtest (Cohort A only), and the100-meter timed test (Cohort B only).
    i. The mean increase from baseline in NSAA score was 5.5 points at 1 year and 7 points at 4 years. However, the open-label design limits interpretability of these clinical outcomes.
    ii. No clear correlation was evident between Elevidys micro-dystrophin expression and clinical outcomes.
- The small sample size and open-label design preclude drawing definitive conclusions regarding efficacy and safety.

2. Trial #2: SRP-9001-102 (Study 102, NCT03769116) was a randomized, double-blind, placebo-controlled trial evaluating Elevidys in 41 ambulatory boys aged 4-7 years with DMD. This trial failed to demonstrate a statistically significant improvement with Elevidys compared to placebo on the primary clinical outcome measure, the North Star Ambulatory Assessment (NSAA), at 48 weeks.
    - The co-primary endpoints were Elevidys micro-dystrophin expression at Week 12 (biomarker) and change in NSAA score from baseline to Week 48 (functional endpoint).
        - Elevidys micro-dystrophin expression was significantly increased compared to placebo. However, there was no statistically significant difference between the Elevidys and placebo groups in change in NSAA score at Week 48.
        - No clear correlation was seen between the level of micro-dystrophin expression and change in NSAA score.
    - Exploratory subgroup analyses hinted at a potential benefit of Elevidys in younger (aged 4-5 years) patients, but subgroup analyses were not prespecified and must be interpreted cautiously.
        - In the younger cohort (aged 4-5 years), there was a numerical advantage in NSAA scores for the ELEVIDYS group.
        - For the older cohort (aged 6-7 years), a numerical disadvantage was observed for ELEVIDYS.
    - Elevidys did not demonstrate improvement compared to placebo on any secondary functional endpoints.
3. Trial #3: SRP-9001-103 (Study 103, NCT04626674) is an ongoing, open-label, multi-center study that encompasses a cohort of 20 ambulatory male DMD subjects aged 4 through 7 years with confirmed mutations in the DMD gene.
    a. The primary objective was to assess Elevidys micro-dystrophin expression at 12 weeks by Western blot.

b. The use of an open-label design does not offer the robustness of blinded, controlled studies in objectively assessing the impact of a treatment.

Medical Necessity Criteria for Elevidys (delandistrogene moxeparvovec-rokl)

Due to insufficient efficacy data, potential safety risks, and the absence of robust clinical efficacy data, the Plan has determined that it does not have established medical necessity criteria for coverage of Elevidys at this time.

1. The primary efficacy endpoint, change in NSAA total score, did not achieve statistical significance in Study 102 (NCT03769116). While there were some numerical advantages in subgroups, the overall data did not convincingly demonstrate a clinically meaningful benefit of Elevidys.
2. In addition, there are uncertainties related to the long-term safety of Elevidys. The product induces high titers of anti-AAV antibodies, with potential implications for immunologic cross-reactivity to other AAV gene therapy products patients may require in the future. The possibility of administering an ineffective one-time gene therapy poses substantial opportunity costs for these patients.

The Plan will reassess our coverage policy as new evidence emerges and ensure that our beneficiaries have access to the most effective and safe treatments for DMD. As always, individual clinical circumstances may warrant exceptions to our general policy position. Such requests for coverage of Elevidys (delandistrogene moxeparvovec-rokl) will be reviewed on a case-by-case basis.

Experimental or Investigational / Not Medically Necessary

Elevidys (delandistrogene moxeparvovec-rokl) for any other indication or use is considered not medically necessary by the Plan, as it is deemed to be experimental, investigational, or unproven. The Plan has reviewed the current clinical evidence and has concluded that Elevidys (delandistrogene moxeparvovec-rokl) for the treatment of Duchenne muscular dystrophy (DMD) is not considered medically necessary at this time due to the following reasons:

1. Inadequate efficacy data across the clinical trials.
2. The inability of Elevidys (delandistrogene moxeparvovec-rokl) to demonstrate a significant and consistent improvement for patients in primary clinical outcomes.
3. Uncertainties surrounding the long-term safety of Elevidys, especially the induction of high anti-AAV antibody levels which may have implications for potential cross-reactivity with other AAV gene therapies in the future.

Given the current evidence and concerns, Elevidys (delandistrogene moxeparvovec-rokl) does not satisfy the Plan's criteria for medical necessity for DMD at this time. The Plan remains committed to providing coverage for a wide range of treatments that have demonstrated both safety and effectiveness based on robust clinical evidence. We will continue to monitor the evolving clinical evidence regarding Elevidys (delandistrogene moxeparvovec-rokl) and will reassess our position as more information becomes available. Until then, we encourage our members to explore alternative treatment options with their healthcare providers.

Applicable Billing Codes (HCPCS/CPT Codes)

Service(s) name	
CPT/HCPCS Codes considered medically necessary if criteria are met:	
Code	*Description*
96365	Intravenous infusion, for therapy, prophylaxis, or diagnosis (specify substance or drug); initial, up to 1 hour
96366	Intravenous infusion, for therapy, prophylaxis, or diagnosis (specify substance or drug); each additional hour (List separately in addition to code for primary procedure)
96367	Intravenous infusion, for therapy, prophylaxis, or diagnosis (specify substance or drug); additional sequential infusion of a new drug/substance, up to 1 hour (List separately in addition to code for primary procedure)
96368	Intravenous infusion, for therapy, prophylaxis, or diagnosis (specify substance or drug); concurrent infusion (List separately in addition to code for primary procedure)
C9399	Unclassified drugs or biologicals
J3490	Unclassified drugs
J3590	Unclassified biologics
ICD-10 codes considered medically necessary if criteria are met:	
Code	*Description*
G71.01	Duchenne or Becker muscular dystrophy

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